American Journal of Medical Genetics 68:70–73 (1997)

Tetramelic Mirror-Image Polydactyly and a De Novo Balanced Translocation Between 2p23.3 and 14q13

Kyoung Chang Kim,[1] Keiko Wakui,[2] Akira Yamagishi,[2] Tsutomu Ohno,[3] Masato Sato,[4] Satohiko Imaizumi,[5] Toshinori Aihara,[6] Yoshimitsu Fukushima,[7] and Hirofumi Ohashi[1]*

[1] *Division of Medical Genetics, Saitama Children's Medical Center, Iwatsuki, Japan*
[2] *Clinical Laboratory Department, Saitama Children's Medical Center, Iwatsuki, Japan*
[3] *Division of Neonatology, Saitama Children's Medical Center, Iwatsuki, Japan*
[4] *Division of Orthopedics, Saitama Children's Medical Center, Iwatsuki, Japan*
[5] *Division of Surgery, Saitama Children's Medical Center, Iwatsuki, Japan*
[6] *Division of Radiology, Saitama Children's Medical Center, Iwatsuki, Japan*
[7] *Department of Hygiene and Medical Genetics, Shinshu University School of Medicine, Matsumoto, Japan*

We report on a male infant with tetramelic mirror-image polydactyly and a de novo, balanced reciprocal translocation between 2p23.3 and 14q13. This patient suggests that a novel gene, which functions in the morphogenesis of the hands and feet along the anterior-posterior axis, may be located at 2p23.3 or 14q13. Am. J. Med. Genet. 68:70–73, 1997 © 1997 Wiley-Liss, Inc.

KEY WORDS: polydactyly; mirror-image; translocation between 2p and 14q; chromosome 2p; chromosome 14q

INTRODUCTION

Mirror polydactyly is a rare limb anomaly characterized by symmetrical duplications of the postaxial digits and ulna/fibula, usually associated with deficiency of thumb/hallux and radius/tibia. Although not much is known about the basic defects causing the mirror polydactyly, genes which regulate the limb patterning along the anterior-posterior axis in embryogenesis might be responsible.

We describe a male infant with tetramelic mirror-image polydactyly associated with a de novo balanced translocation between 2p and 14q.

CLINICAL REPORT

The patient (5-9153-5), a boy, was born at 32 weeks of gestation to a 27-year-old G2P2 mother and 29-year-old father, both healthy and unrelated. The pregnancy and labor were uneventful. There was no family history of malformations. His birth weight was 2,326 g (+1.5 S.D.), length 42.6 cm (0.0 S.D.), and OFC 30.2 cm (+0.4 S.D.). He had a left inguinal hernia and tetramelic polydactyly. There were six fingers on each hand, with cutaneous syndactyly between the 2nd and 3rd fingers on the right. None appeared to be a thumb. All fingers had nails. Eight toes were present on each foot. All toes, except the most tibial toe on the right, had nails. The hallux cannot be identified on either foot (Fig. 1). The arms and legs were normal in length and shape. Radiologically, each hand had six metacarpals. All fingers had three phalanges, except the 1st finger on the left with two phalanges. The left foot had eight metatarsals, and the right had seven. On the left foot, the 1st toe had two phalanges, the eighth two, and the others three. On the right, the 1st toe had no phalanx, the 8th two, and the others three (Fig. 2). The long bones of the arms and legs were normal. At age 4 months, no apparent delay in his growth and motor development was noted.

G-banding studies using peripheral blood lymphocytes showed that the patient had a reciprocal translocation between the short arm of chromosome 2 and the long arm of chromosome 14. High resolution analysis using a modified ethidium bromide technique [Ikeuchi and Sasaki, 1979] indicated that the breakpoints of this translocation were 2p23.3 and 14q13 (Fig. 3). The translocation seemed to be balanced with no apparent chromosome deletions or duplications around the breakpoints. The parents were chromosomally normal. Therefore, the karyotype of the patient was interpreted as 46,XY,t(2;14)(p23.3;q13)de novo.

DISCUSSION

The early development of limbs in embryogenesis is considered to proceed along the following three axes: (1) proximal-distal (P-D), (2) dorsal-ventral (D-V), and (3) anterior-posterior (A-P). Mirror polydactyly seems to result from a disturbance of limb pattern formation in the A-P axis. Thus far, several genes are assumed to be responsible for limb development along the A-P axis: (1) genes (unidentified yet) related to the Sonic hedgehog expression [Riddle et al., 1993], and (2) the Homeobox-D (HoxD) gene [Morgan and Tabin, 1993]. They are

Contract grant sponsor: the Ministry of Health and Welfare for Pediatric Research, contract grant number: 7C-1; Contract grant sponsor: the Ministry of Health and Welfare for Nervous and Mental Disorders, contract grant number: 7A-5; Contract grant sponsor: Kawano Memorial Foundation for Promotion of Pediatrics

* Correspondence to: Hirofumi Ohashi, M.D., Ph.D., Division of Medical Genetics, Saitama Children's Medical Center, 2100 Magome, Iwatsuki, Saitama 339, Japan.

Received 13 December 1995; Accepted 8 March 1996

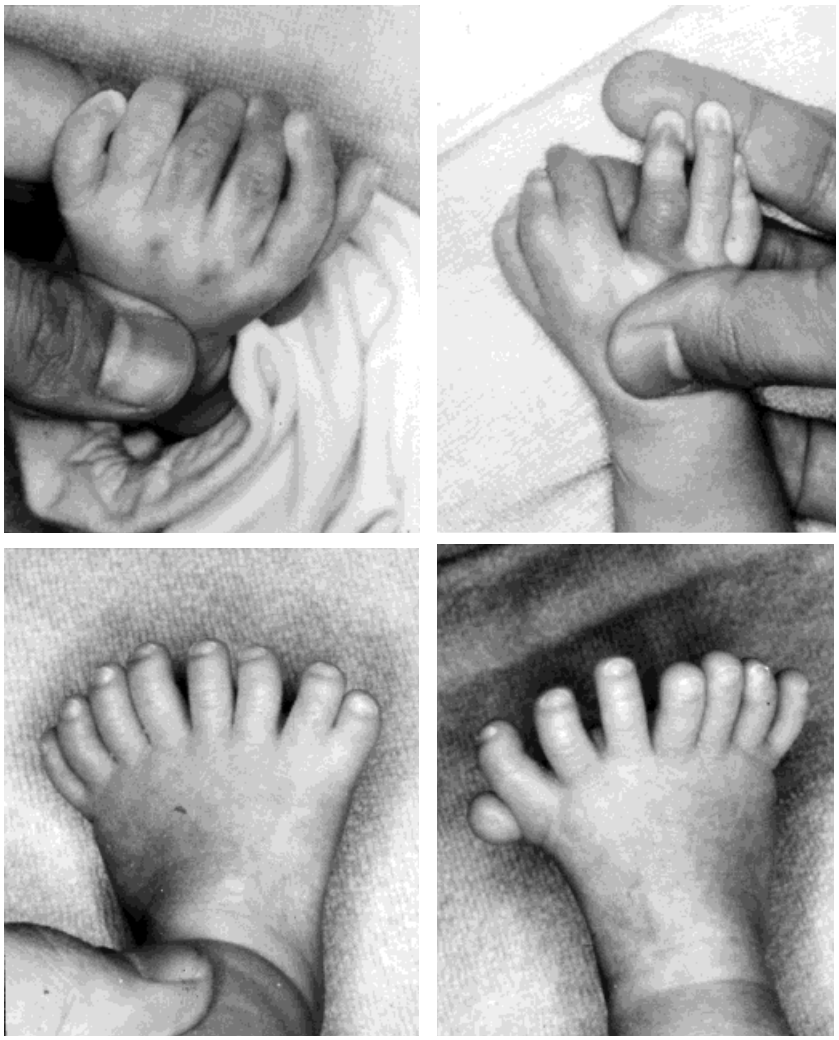

Fig. 1. Mirror-image polydactyly.

considered to be expressed in the zone of polarizing activity in the developing limb bud mesoderm, which determines polarity of the A-P axis. Other candidates are the bone morphogenetic protein (BMP)-2 and -4 genes, which are expressed in and around chondrogenic regions and functions in the molding of bones of limb elements such as digits. The reported chromosomal locations of HoxD gene [Boncinelli et al., 1988] and BMP-2 gene [Rao et al., 1992] are different from the breakpoints (2p23.3 and 14q13) involved in the translocation of our patient. The BMP-4 gene is recently reported to be mapped on chromosome 14q22–q23 [Tabaset al., 1993; Van den Wijngaard et al., 1995].

Tetramelic polydactyly in the present patient can not be classified as "classic" mirror polydactyly since his postaxial long bones in the forearms and the lower legs are not duplicated [Groper, 1983]. We are aware of two similar patients previously reported. Martin et al. [1993] reported on a father and daughter with mirror-image polydactyly and a distinct nasal defect with no long bone defect in the forarms and the legs. Barton et al. [1986] described a patient with bilateral mirror-image polydactyly and absent thumbs without ulnar dimelia, who had a family history of polydactylism in a dominant pattern.

In conclusion, this patient suggests that a novel gene responsible for the patterning of hands and feet along the A-P axis in embryogenesis may be located at 2p23.3 or 14q13.

ACKNOWLEDGMENTS

We express our thanks to Professor Norio Niikawa and Dr. Naomichi Matsumoto for their valuable advice and Professor Scott W. Eberle for his reading and correcting the manuscript. This work was supported in part by Grants for Pediatric Research (7C-1) and for Nervous and Mental Disorders (7A-5) from the Ministry of Health and Welfare and by a Grant-in-Aid

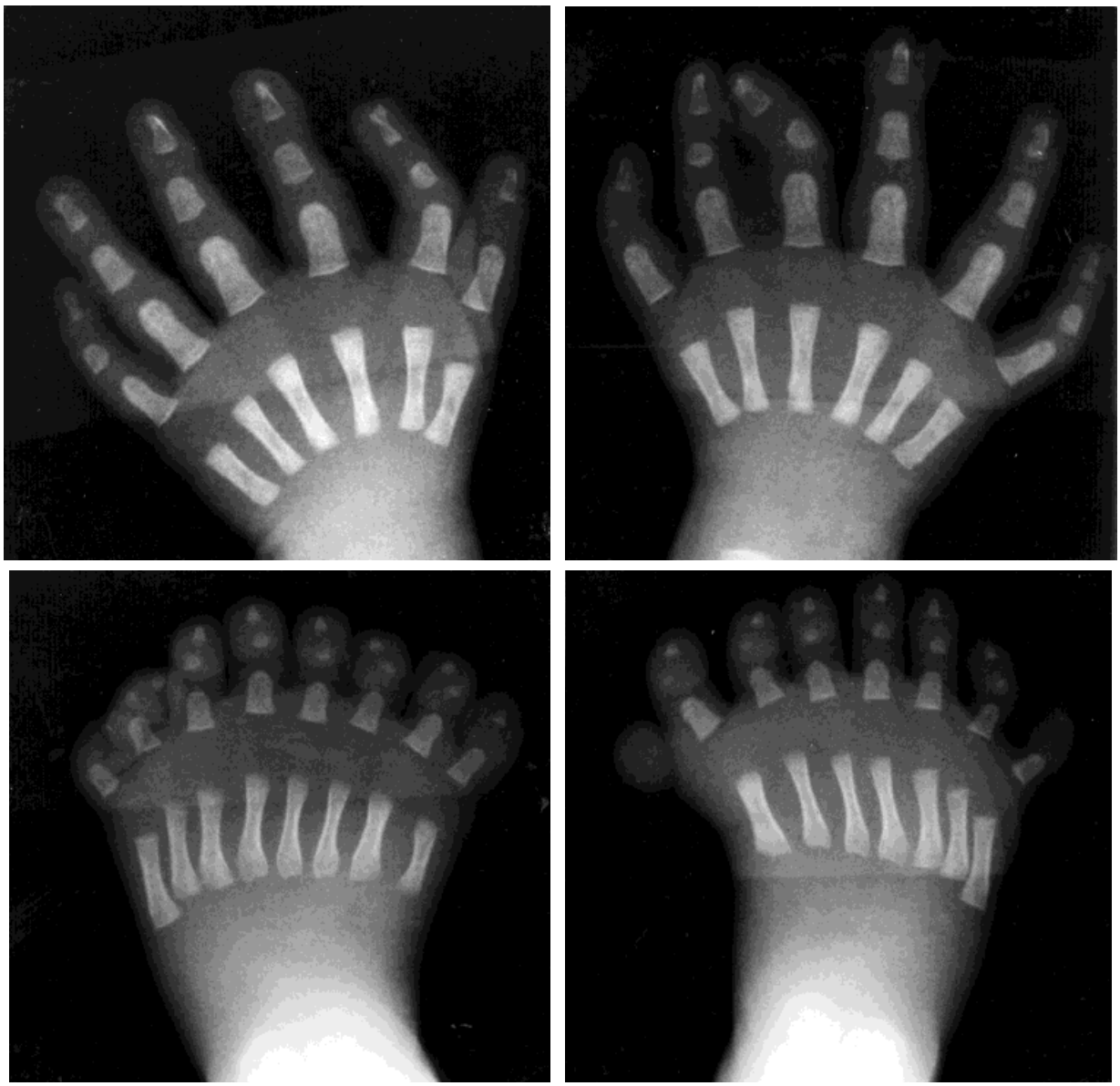

Fig. 2. Radiographs of hands and feet.

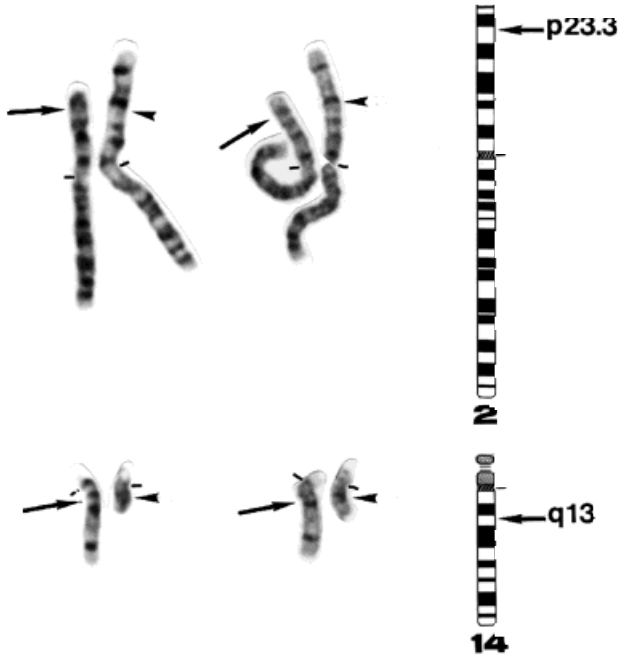

Fig. 3. Two sets of high-resolution G-banded chromosomes 2 and 14 of the patient. The upper row shows chromosome 2 and the lower chromosome 14. Each arrow indicates a breakpoint on the normal chromosome and each arrowhead a rejoining point of the rearranged chromosome. Breakpoints are 2p23.3 and 14q13.

from the Kawano Memorial Foundation for Promotion of Pediatrics.

REFERENCES

Barton NJ, Buck-Gramcko D, Evans DM (1986): Soft-tissue anatomy of mirror hand. J Hand Surg 11:307–319.

Boncinelli E, Somma R, Acampora D, Pannese M, D'Esposito M, Faiella A, Simeone A (1988): Organization of human homeobox genes. Hum Reprod 3:880–886.

Groper P (1983): Ulnar dimelia. J Hand Surg 8:487–491.

Ikeuchi T, Sasaki M (1979): Accumulation of early mitotic cells in ethidium bromide-treated human lymphocyte cultures. Proc Jpn Acad 55:15–18.

Martin RA, Jones MC, Jones KL (1993): Mirror hands and feet with a distinct nasal defect, an autosomal dominant condition. Am J Med Genet 46:129–131.

Morgan BA, Tabin CJ (1993): The role of homeobox genes in limb development. Curr Biol 3:668–674.

Rao VVNG, Loffler C, Wozney JM, Hansmann I (1992): The gene for BMP2A is localized to human chromosome 20p12 by radioactive and non-radioactive in situ hybridization. Hum Genet 90: 299–302.

Riddle RD, Johnson RL, Laufer E, Tabin C (1993): Sonic hedgehog mediates the polarizing activity of the ZPA. Cell 75:1401–1416.

Tabas JA, Hahn GV, Cohen RV, Seaunex HN, Modi WS, Wozney JM, Zasloff M, Kaplan FS (1993): Chromosomal assignment of the human gene for bone morphogenetic protein 4. Clin Orthop 293: 310–316.

Van den Wijngaard A, Weghuis DO, Boersma CJC, Van Zoelen EJJ, Van Kessel AG, Olijve W (1995): Fine mapping of the human bone morphogenetic protein-4 gene (BMP4) to chromosome 14q22–q23 by in situ hybridization. Genomics 27:559–560.